REMARKS

Claims

Claims 1–18 are pending.

Rejections under 35 U.S.C. §112,¶1

Claims 1, 3–11 and 13–18 are rejected under §112, ¶1 as allegedly being failing to provide enablement. This rejection is respectfully traversed.

The basis for this rejection is stated at page 2 of the outstanding Office Action, wherein it is alleged that "the specification, while being enabling for antagonizing the EP_2 receptors by EP2 antagonists, does not provide enablement for other antagonizing methods." Applicants disagree with this contention.

At page 2 of the outstanding Office Action, the rejection begins with a recitation of the so-called *Wands* factors. The Examiner asserts that these are the factors to consider when determining whether a disclosure satisfies the enablement requirement under 35 U.S.C. §112, ¶1. However, this is not an accurate description of the analysis of the *Wands* factors.

The Wands factors are to be used for determining whether undue experimentation is required for enablement. As expressly stated by the court in *In re Wands*, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988), "Factors to be considered in determining whether a disclosure would require undue experimentation have been summarized in *Ex parte Forman*. They include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, ..." However, before the issue of undue experimentation arises, the rejection first must present reasons to doubt the veracity of the enablement statements presented in the specification.

Applicants' specification, coupled with a skilled worker's knowledge, provides more than adequate guidance on how to practice the claimed methods using the molecules recited in the claims. The specification provides both general and specific guidance regarding the EP2 receptor antagonists and Cox-2 inhibitors. Combinations and compositions comprising such molecules, and the utility thereof, for example, in impairing cumulus expansion and oocyte maturation, are also described. See, for example, the disclosure contained in the paragraphs bridging page 7, line 25 to page 8, line 23 of the instant specification. See also the experimental data provided in the enclosed declaration.

As clearly and succinctly stated by the court in *In re Marzocchi*, 169 USPQ 367, 369 (CCPA 1971):

> As a matter of Patent Office practice, then a specification disclosure which contains a teaching of the manner and process of making and using the invention in terms which correspond in scope to those used in describing and defining the

> subject matter sought to be patented **must** be taken in compliance with the enabling requirement of the first paragraph of §112, **unless** there is reason to doubt the objective truth of statements contained therein relied on for enabling support. (emphasis in original)

Furthermore, as stated in *Marzocchi*, at 370, the PTO must have adequate support (evidence or reasoning) for its challenge to the credibility of Applicants' statements of enablement. Thus, in the absence of evidence which demonstrates otherwise, the claims must be taken to satisfy the requirements of 35 U.S.C. § 112, ¶1.

In the instant case, the rejection rests on the allegation that "other antagonizing methods" are not enabled by the present specification. While the Office Action concedes that the present specification provides an enabling disclosure on EP2 receptor antagonists, such as, for example, AH6809 compound of claim 2. However, the Office Action fails to provide a single example of what such "other antagonizing methods" constitute. As such, the rejection is without merit.

A skilled worker knows and understands that antagonism purports to "counteraction," such as, for example, against the biological activity of a receptor. For a skilled worker who possesses adequate knowledge on EP2 receptor proteins and activity thereof, receptor antagonism is well-understood. For example, molecules can be targeted to disrupt ligand-receptor interactions or intracellular signaling pathways. The references cited in, for example, page 7 of the present specification provide representative examples of such techniques. As such, adapting such molecules for EP2 receptor antagonism would be nothing more than routine to one of ordinary skill in the art. Further demonstration that the molecules of the present invention are functional *in vivo* is provided by the declaration enclosed herewith. It is therefore respectfully submitted that Applicants' disclosure more than adequately meets the statutory requirements under §112, ¶1.

In discussing the *Wands* factors, the rejection generally asserts that the pharmaceutical art is unpredictable, "requiring each embodiment to be physically assessed for physiological activity." These allegations are baseless. In any event, the Office Action fails to present any evidence to doubt the objective enablement of Applicants' disclosure. A general assertion of unpredictability does not provide reasons to doubt the veracity of the statements in Applicants' specification with respect to scope of the present claims. At page 7, ¶2, the Office Action cites lack of working examples. It is respectfully submitted that working examples are not required to establish enablement. As stated by the court *Marzocchi*, at page 369:

> The first paragraph of §112 requires nothing more than objective enablement. How such a teaching is set forth, either by the use of illustrative examples or by broad terminology, is of no importance. (Emphasis added)

The assertion of undue experimentation (see, page 3 of the Office Action) in the rejection is

merely conclusory, and absent supporting disclosures to support such assertions, the rejection based on such a premise is without legal merit. The Office Action fails to provide a single supporting publication to support the contention that the claims include compounds of "various structural formulas requiring specific EP2 antagonist activity." Moreover, the requirement that Applicants "establish, by individual assay, each compound deemed suitable in the instant invention" is legally misplaced. The courts have routinely held that the presence of inoperative embodiments within the scope of a claim does not render a claim non-enabled. The standard is whether a skilled person could determine which embodiments that were conceived, but not yet made, would be inoperative or operative with expenditure of no more effort than is normally required in the art. Atlas Powder Co. v. E.I. du Pont de Nemours & Co., 750 F.2d 1569, 1577, 224 USPQ 409, 414 (Fed. Cir. 1984); MPEP 2164.08(b). The specification provides clear guidance on how to routinely test for and use the EP2 antagonists in their broadest possible scope. Withdrawal of the rejection is respectfully requested.

Rejections under 35 U.S.C. §103(a)

Claims 1–18 are rejected under §103(a) as allegedly being rendered obvious by the teachings of Breyer (*Annals of NY Academy of Sciences*, 2000) in view of Narumiya (*Physiological Reviews*, 1999), Hizaki (*PNAS*, 1999), Norel (*BJP*, 1999) further in view of Noble (*American Family Physician*, 2000). This rejection is respectfully traversed.

Applicants respectfully submit that in view of Dr. Lindenthal's declaration under 37 CFR §1.132, which is enclosed herewith, any issue of *prima facie* case of obviousness is moot. The experimental data enclosed herewith provides additional corroborating scientific evidence that the claimed combination of EP2 antagonists and Cox-2 inhibitors is unobvious over the art cited references. The declaration clearly demonstrates that treatment with EP2 antagonist (ZK6073610) and COX-2 inhibitor (Rofecoxib) led to a reduction of fertilization factor *in vivo*. The declaration further demonstrates that combinations of an EP2-antagonist with a Cox-2 inhibitor unexpectedly and significantly reduce the fertilization factor. In addition, the maximal *in vivo* effect achievable with a Cox-2 inhibitor can be increased by co-administration of an EP2-antagonist, even when low doses of Cox-2 inhibitors are administered. See, for example, the figures/data of the enclosed Lindenthal declaration.

In view of the above remarks, favorable reconsideration is courteously requested. If there are any remaining issues which could be expedited by a telephone conference, the Examiner is courteously invited to telephone counsel at the number indicated below.

The Commissioner is hereby authorized to charge any fees associated with this response to Deposit Account No. 13-3402.

Respectfully submitted,

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